13/12/200416:13Print selected from Online session

FILE 'HOME' ENTERED AT 15:59:07 ON 13 DEC 2004

=> index bioscience
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, ANTE, AQUALINE, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOENG, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU, DGENE, DISSABS, ...' ENTERED AT 15:59:27 ON 13 DEC 2004

75 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> (Factor (w) VIII) (p)(polyethylene (w) glycol)
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          0*  FILE ADISNEWS
          0*  FILE ANTE
          0*  FILE AQUALINE
          0*  FILE BIOCOMMERCE
          3*  FILE BIOENG
         22   FILE BIOSIS
         14*  FILE BIOTECHABS
         14*  FILE BIOTECHDS
          6*  FILE BIOTECHNO
          1   FILE CANCERLIT
         49   FILE CAPLUS
          0*  FILE CEABA-VTB
          1   FILE CEN
          0*  FILE CIN
          1   FILE DDFU
  26 FILES SEARCHED...
          1   FILE DISSABS
          2   FILE DRUGU
         16   FILE EMBASE
          2*  FILE ESBIOBASE
          0*  FILE FEDRIP
          0*  FILE FOMAD
          0*  FILE FOREGE
          0*  FILE FROSTI
          0*  FILE FSTA
         48   FILE IFIPAT
          2   FILE IMSDRUGNEWS
          1   FILE IMSRESEARCH
          1   FILE JICST-EPLUS
          0*  FILE KOSMET
          3   FILE LIFESCI
          0*  FILE MEDICONF
  49 FILES SEARCHED...
         15   FILE MEDLINE
          0*  FILE NTIS
          0*  FILE NUTRACEUT
          5*  FILE PASCAL
          1*  FILE PHARMAML
          2   FILE PROMT
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          7   FILE SCISEARCH
         20   FILE TOXCENTER
        101   FILE USPATFULL
          1   FILE USPAT2
          0*  FILE WATER
         39   FILE WPIDS
  73 FILES SEARCHED...
         39   FILE WPINDEX

  28 FILES HAVE ONE OR MORE ANSWERS,   75 FILES SEARCHED IN STNINDEX

L1   QUE (FACTOR (W) VIII) (P)(POLYETHYLENE (W) GLYCOL)

=> ((Factor (w) VIII) (p)( polyethylene (w) glycol)) and "10000 daltons"
          0*  FILE ADISNEWS
          0*  FILE ANTE
          0*  FILE AQUALINE
          0*  FILE BIOCOMMERCE
          0*  FILE BIOENG
          0*  FILE BIOTECHABS
          0*  FILE BIOTECHDS
          0*  FILE BIOTECHNO
          0*  FILE CEABA-VTB
          0*  FILE CIN
  25 FILES SEARCHED...
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          0*  FILE FEDRIP
          0*  FILE FOMAD
          0*  FILE FOREGE
          0*  FILE FROSTI
          0*  FILE FSTA
  46 FILES SEARCHED...
          0*  FILE KOSMET
          0*  FILE MEDICONF
          0*  FILE NTIS
          0*  FILE NUTRACEUT
          0*  FILE PASCAL
          0*  FILE PHARMAML
  67 FILES SEARCHED...
          0*  FILE WATER

   0 FILES HAVE ONE OR MORE ANSWERS,   75 FILES SEARCHED IN STNINDEX

L2   QUE ((FACTOR (W) VIII) (P)(POLYETHYLENE (W) GLYCOL)) AND "10000 DALTONS"

=> file biosis medline caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                               3.99       4.20

FILE 'BIOSIS' ENTERED AT 16:03:31 ON 13 DEC 2004
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FILE 'MEDLINE' ENTERED AT 16:03:31 ON 13 DEC 2004

FILE 'CAPLUS' ENTERED AT 16:03:31 ON 13 DEC 2004
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=> (Factor (w) VIII) (p)(polyethylene (w) glycol)
L3 86 (FACTOR (W) VIII) (P)(POLYETHYLENE (W) GLYCOL)

=> dup remove
ENTER L# LIST OR (END):L3
PROCESSING COMPLETED FOR L3
L4 59 DUP REMOVE L3 (27 DUPLICATES REMOVED)

=> L4 and daltons
L5 1 L4 AND DALTONS

=> d ti

L5 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI FACTORS AFFECTING THE RELATIVE DISTRIBUTION OF HIGH AND LOW MOLECULAR WEIGHT FORMS OF FACTOR-VIII.

=> d ab bib

L5 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AB In heparinized [human] plasma, approximately 50% of the **factor VIII** procoagulant activity has a very low molecular weight (VLMW) of approximately 20,000. The balance of the procoagulant activity is in a high MW form (HMW) which is associated with the carrier protein (VIII:RAG). **Factor VIII** which was purified from citrated plasma has a MW of about 106 **daltons** and can be separated after CaCl2 dissociation into a HMW carrier (VIII:RAG, MW 106) and a low MW procoagulant component (LMW, MW 150,000). The factors which influence the aggregation of the native VLMW form of **factor VIII** were studied. The ratio of VLMW:HMW in heparinized plasma is 1:1 and decreases to 1:5 when CPD [citrate-posphate-dextrose] is used as anticoagulant. VLMW is not detectable in EDTA plasma. The collection of blood into heparin and granuated amounts of CPD results in an increased proportion of VLMW as the CPD concentration is reduced. The ratio of VLMW:HMW remains constant at 1:1 during storage of the heparinized plasma but decreases to almost 0:1 after 24 h in citrated plasma. When separated from HMW, the VLMW alone aggregates on storage at -80° C for 72 h producing forms of intermediate MW although the majority of the activity is in a HMW form. This aggregated VLMW material is devoid of VIII:RAG and dissociates into low and high MW peaks following chromatography with buffer containing 0.25 M CaCl2. Cryoprecipitation and PEG [**polyethylene glycol**] precipitation of heparinized plasma shift the VLMW:HMW ratio from 1:1 to 0:1. The usual conditions of storage and processing of plasma result in the aggregation of the normal VLMW to HMW forms which are artifacts of the isolation process, and are further evidence against the one-molecule theory of **factor VIII** structure.
AN 1979:262574 BIOSIS
DN PREV197968065078; BA68:65078
TI FACTORS AFFECTING THE RELATIVE DISTRIBUTION OF HIGH AND LOW MOLECULAR WEIGHT FORMS OF FACTOR-VIII.
AU ROCK G A [Reprint author]; PALMER D S; TACKABERRY E S
CS FAC MED, UNIV OTTAWA, OTTAWA, ONT K1N 6N5, CAN
SO Thrombosis Research, (1979) Vol. 14, No. 4-5, pp. 573-588.
CODEN: THBRAA. ISSN: 0049-3848.
DT Article
FS BA

LA ENGLISH

=> L4 and "molecular Weight"
L6 7 L4 AND "MOLECULAR WEIGHT"

=> d ti 1-7

L6 ANSWER 1 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI Effects of high-**molecular-weight** cryoprotectants on platelets and the coagulation system.

L6 ANSWER 2 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI CONDITIONS AFFECTING THE **MOLECULAR WEIGHT** OF FACTOR-VIII.

L6 ANSWER 3 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI FACTORS AFFECTING THE RELATIVE DISTRIBUTION OF HIGH AND LOW **MOLECULAR WEIGHT** FORMS OF FACTOR-VIII.

L6 ANSWER 4 OF 7 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI PURIFICATION OF LOW **MOLECULAR WEIGHT** FACTOR-VIII BY AFFINITY CHROMATOGRAPHY USING FACTOR-VIII SEPHAROSE.

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
TI Isolation of albumin from plasma products by fractionation

L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
TI Subunit structure of normal and hemophilic factor VIII

L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
TI Isolation and characterization of bovine factor VIII (antihemophilic factor)

=> L4 and covalent
L7 0 L4 AND COVALENT

=> L4 and conjugate
L8 4 L4 AND CONJUGATE

=> d ti 1-4

L8 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
TI B-domain deleted recombinant coagulation **factor VIII** modified with monomethoxy **polyethylene glycol.**

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Poly(alkylene oxide)-blood coagulation factor VIII or factor IX **conjugates**

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Pharmaceutical composition comprising factor VIII and neutral liposomes

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
TI Blood-coagulation factor VIII **conjugates**

=> d ab bib 1-4

L8 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AB Recombinant coagulation factor VIII (r-VIII SQ) was chemically modified with monomethoxy poly-(ethylene glycol) (mPEG). Three mPEG derivatives were used for coupling to the r-VIII SQ lysines, a mixed anhydride of monomethoxy poly(ethylene glycol) succinic acid (mPEG-SAH), monomethoxy poly(ethylene glycol) succinimidyl succinate (mPEG-SS), and monomethoxy poly(ethylene glycol) tresylate (mPEG-TRES). A consequence of the modification with all derivatives was a substantial reduction in coagulant activity, even at very low degrees of modification. A method was developed with the purpose of avoiding conjugation at certain important biological sites on the factor VIII and thereby producing **conjugates** with better retained activity. This was achieved by immobilizing the protein onto a solid matrix during the modification reaction. Characterization of **conjugates** by SDS-PAGE, western blots, interaction with von Willebrand factor (vWf), and thrombin activation/inactivation analyses was undertaken. The SDS-PAGE and western blots revealed coupling heterogeneity regarding degree of modification. The amount of factor VIII able to bind to vWf decreased with the conjugation. Thrombin activated the modified factor VIII to essentially the same extent as the reference preparation of r-VIII SQ. Inactivation of the modified factor VIII was, however, slower than inactivation of the unmodified protein. Finally, an in vitro study was performed to evaluate the influence of the mPEG modification on the protein stability in extract of porcine tissue. Despite that **conjugates** with low degrees of modification were included in the study, the coagulant activity was preserved to a significantly higher extent in all incubation mixtures containing **conjugates** compared to that with unmodified protein.
AN 2000:368985 BIOSIS
DN PREV200000368985
TI B-domain deleted recombinant coagulation **factor VIII** modified with monomethoxy **polyethylene glycol**.
AU Rostin, Johanna; Smeds, Anna-Lisa; Akerblom, Eva [Reprint author]
CS Department of Organic Pharmaceutical Chemistry, Uppsala Biomedical Center, S-751 23, Uppsala, Sweden
SO Bioconjugate Chemistry, (May-June, 2000) Vol. 11, No. 3, pp. 387-396. print.
CODEN: BCCHES. ISSN: 1043-1802.
DT Article
LA English
ED Entered STN: 30 Aug 2000
Last Updated on STN: 8 Jan 2002

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
AB Blood-coagulation factor VIIIC:von Willebrand factor, factor VIII:C, or factor IX or the activated factors are covalently linked to a poly(alkylene oxide). The resulting **conjugates** have improved stability and decreased immunogenicity.
AN 2000:169386 CAPLUS
DN 132:212666
TI Poly(alkylene oxide)-blood coagulation factor VIII or factor IX **conjugates**
IN Minamino, Hitoshi; Mealey, Edward H.
PA Alpha Therapeutic Corporation, USA
SO U.S., 6 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6037452	A	20000314	US 1992-866518	19920410
PRAI	US 1992-866518		19920410		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AB A pharmaceutical composition for parenteral administration comprising a therapeutically effective amount of a protein or polypeptide and substantially neutral colloidal particles. The particles comprise approx. 1-20 mol% of an amphipathic lipid derivatized with a biocompatible hydrophilic polymer which carries substantially no net charge. The protein or polypeptide is capable of externally binding the colloidal particles, or is capable of binding PEG, and is not encapsulated in the colloidal particles. A preferred protein is **factor VIII** , whose half-life is extended and which is protected from serum inhibitor antibodies by injecting it as a component of the composition Egg phosphatidylcholine (EPC) and distearoylphosphatidylethanolamine-Me **polyethylene glycol** 2000 (DSPE-PEG 2000) were weighed i.m. a ratio of 80:20 (5% molar ratio of DSPE-PEG 2000), resp., dissolved in 10% in tert-BuOH, and the solution was lyophilized. The dry lipid powder obtained was resuspended at 10% in a buffer containing 130 mM NaCl, 10 mM sodium citrate, pH 7.0 1 mM CaCl2 to form liposomes. The liposomes were filtered in an extruder apparatus through polycarbonate filters (1.2, 0.2 and 0.1 μm) to form liposomes (120-140 nm). The **factor VIII** was formulated into liposomes and the pharmacokinetic parameters were determined

AN 1999:708582 CAPLUS

DN 131:327532

TI Pharmaceutical composition comprising factor VIII and neutral liposomes

IN Baru, Moshe; Bar, Liliana; Nur, Israel

PA Opperbas Holding B.V., Neth.

SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9955306	A1	19991104	WO 1999-IL217	19990423
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2329768	AA	19991104	CA 1999-2329768	19990423
	AU 9934414	A1	19991116	AU 1999-34414	19990423
	AU 747391	B2	20020516		
	BR 9909978	A	20001226	BR 1999-9978	19990423
	EP 1079805	A1	20010307	EP 1999-916022	19990423
	EP 1079805	B1	20041124		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002512947	T2	20020508	JP 2000-545506	19990423

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	US 6593294	B1	20030715	US 2000-673412	20001122
	US 2003134778	A1	20030717	US 2002-327970	20021226
PRAI	IL 1998-124224	A	19980427		
	WO 1999-IL217	W	19990423		
	US 2000-673412	A3	20001122		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN

AB The blood-coagulation **factor VIII** is conjugated to nonantigenic ligands, such as polysaccharides, sialic acid, albumin, von Willebrand factor and **polyethylene glycol**. **Factor VIII** was coupled to NaIO4- oxidized dextran in 1M NaCl and 0.05 M NaAcO, at pH 6. When infused into the bloodstream of hemophilic dogs the conjugated **factor VIII** had longer half-life than the native **factor VIII**.

AN 1991:214411 CAPLUS

DN 114:214411

TI Blood-coagulation factor VIII **conjugates**

IN Fulton, Anne J.; Johnson, Alan J.

PA New York University, USA

SO U.S., 13 pp. Cont.-in-part of U.S. 4,847,362.
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4970300	A	19901113	US 1989-298413	19890118
	US 4743680	A	19880510	US 1985-697267	19850201
	US 4847362	A	19890711	US 1987-122372	19871119
	US 4952675	A	19900828	US 1988-291516	19881229
PRAI	US 1985-697267	A1	19850201		
	US 1987-122372	A2	19871119		

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	34.72	38.92

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.10	-2.10

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